حواف مرتفعة حالي
LA

(14) دائرة حمد

Urticaria

Def Vascular Reaction of Skin ch. BY formation of **Wheals** شخفي ?? (Hives)

4E — Elevated, Edematous, Erythematous, Evanescent (Lasting upto 24 hrs) papules & plaques wh may be ass. c̄ → Itching, Pricking, Stinging

أسبب — Cause by: localized dermal edema (VD)

حوالي & surrounded by Flare (local axon reflex by Neuropeptides)

تجمع — Coalescence of multiple lesions + Central clearing → Annular or Polycyclic pattern.

معاها — May be Accompanied by S.C swelling (Angioedema) that may affect:
- distensable skin: Eyelid & genitalia.
- MM: . GIT → abd. pain
  . RT → asthma & airway obst.

Q مهم ممكن شفوي أو تحريري

Pathomechanisms of urticaria

(dse of Mast cells)

Certain Agents or stimuli → By: Idiopathic / Immunologic or / Non Immunologic — Mechanisms →

Release of Mediators → urticaria (↑ Capillary permeability)

سيتم مناقشة كل خطوة

1. stimuli (Triggers) [ingestant, injectant, inhalant, Inf., ... **4I** [See Types of urticaria]
2. Mechanisms
3. Mediators
4. urticaria.

* Mechanisms of Urticaria and Angioedema (AAFP) (ميكانزم Mast Cells)

1- Immunologic causes: -

(A) *Type I IgE-mediated (أكثر نوع)
- Foods: tree nuts, legumes, crustacea, mollusks, fish, eggs, milk, soy, wheat
- Organic substances: preservatives, latex, hymenoptera venom
- Medications: penicillin, cephalosporin, aspirin, NSAIDs
- Aeroallergens: dust mites, pollens, molds, animal dander

drugs →

also ← Atopy, Anaphylaxis

(B) Autoimmune urticaria: Autoabs against FcεR or Fc of IgE.

2- Nonimmunologic causes = (Pseudoallergic)
- Direct mast cell degranulation: opiates (codein), vancomycin (Vancocin), radiocontrast, Aspirin, Opro media, dextran, muscle relaxants, bile salts, stem cell factor.
- Vasoactive stimuli eg. Nettle stings. العرس اللاسع → direct cut. VD جرثومي استاكوزا
- Foods containing high levels of histamines: strawberries, tomatoes, shrimp, lobster, cheese, spinach, eggplant سبانخ باذنجان
الفراولة-الطماطم-السبانخ-الجبنة-السبانخ-الباذنجان-الجمبري-السمك-التونة-اللحمة

Anti Cox → Drugs
- Cycloxygenase inhibitors: NSAIDs and Aspirin. (cox, pseudoallergic) ↓PGE2 : inhibiter of degranulate. ↑PGD2 & leukotries → urticaria
- ACEI. → ↑ Kinins → VD
- Physical stimuli: exposure to sun, water, or temperature extremes; delayed pressure (e.g., wearing a heavy backpack); vibration

Pseudo allergi Ur

* Mediators of urticaria May be.

Mast cell derived

Preformed (cytoplasmic derived)
- Histamine
- Heparine
- Tryptase
- Chymase

] Proteases

Newly formed (Lipid membrane derived)
- Prostaglandins D2 (PGD2)
- Leukotrienes C4, D4, E4 → Eosinophil
- PAF

- Cytokines
  - IL 3, 4, 5, 6, 8, 13
  - TNF-α
  - GM-CSF

- Substance P.
- Complement
- Kinins

NB
- Tryptase & Chymase: C3 → C3a & C3b
  - C3a → ++ Mast Cells
  - C3b → ++ alternative Complement pathway
- Chymase → degranulation of mast Cells

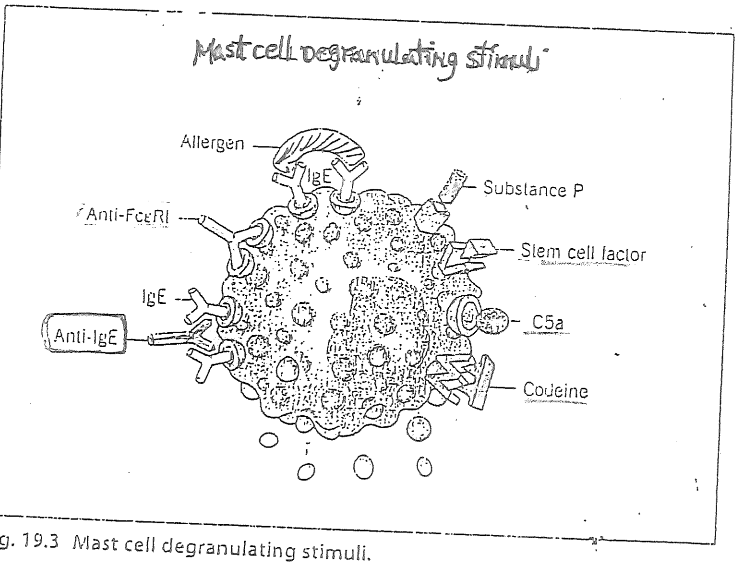
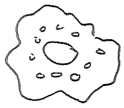


Fig. 19.3 Mast cell degranulating stimuli.

Mast Cell
شبه
Fried egg



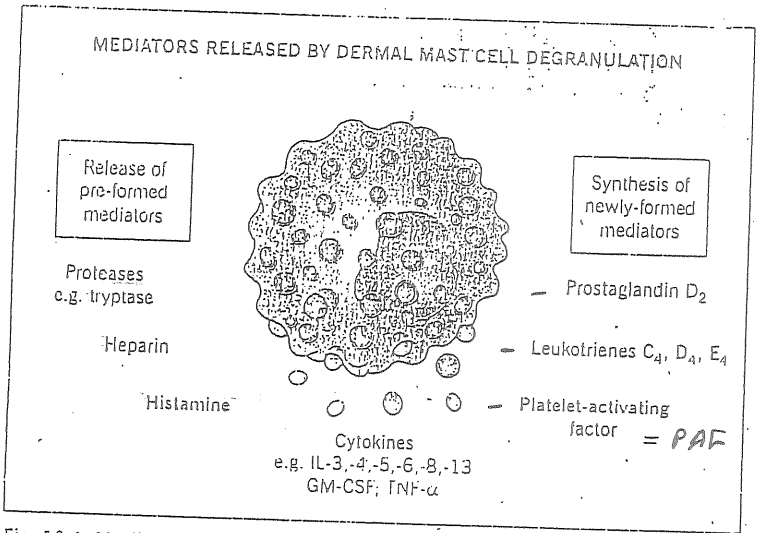


Fig. 19.4 Mediators released by dermal mast cell degranulation. Preformed & newly synthesized proinflammatory mediators in mast cells.

أعطيه Montelocast Singulare مضاد ليه
↓

NB. **Aspirin & urticaria:** (– Cycloxygenase enz (COX) ⟵ ↑ leukot. ↑ PGD2, ↓ PGE synth → urticaria)

- rarely cause urticaria in ℓ individuals
- but it → ↑ Whealing in pts of chr. urticaria during disease activity.
- So it act as a non specific exacerbating factor rather than a direct cause.

لو هاستعمل مسكن يفضل Paracetamol (Weak AntiCOX).

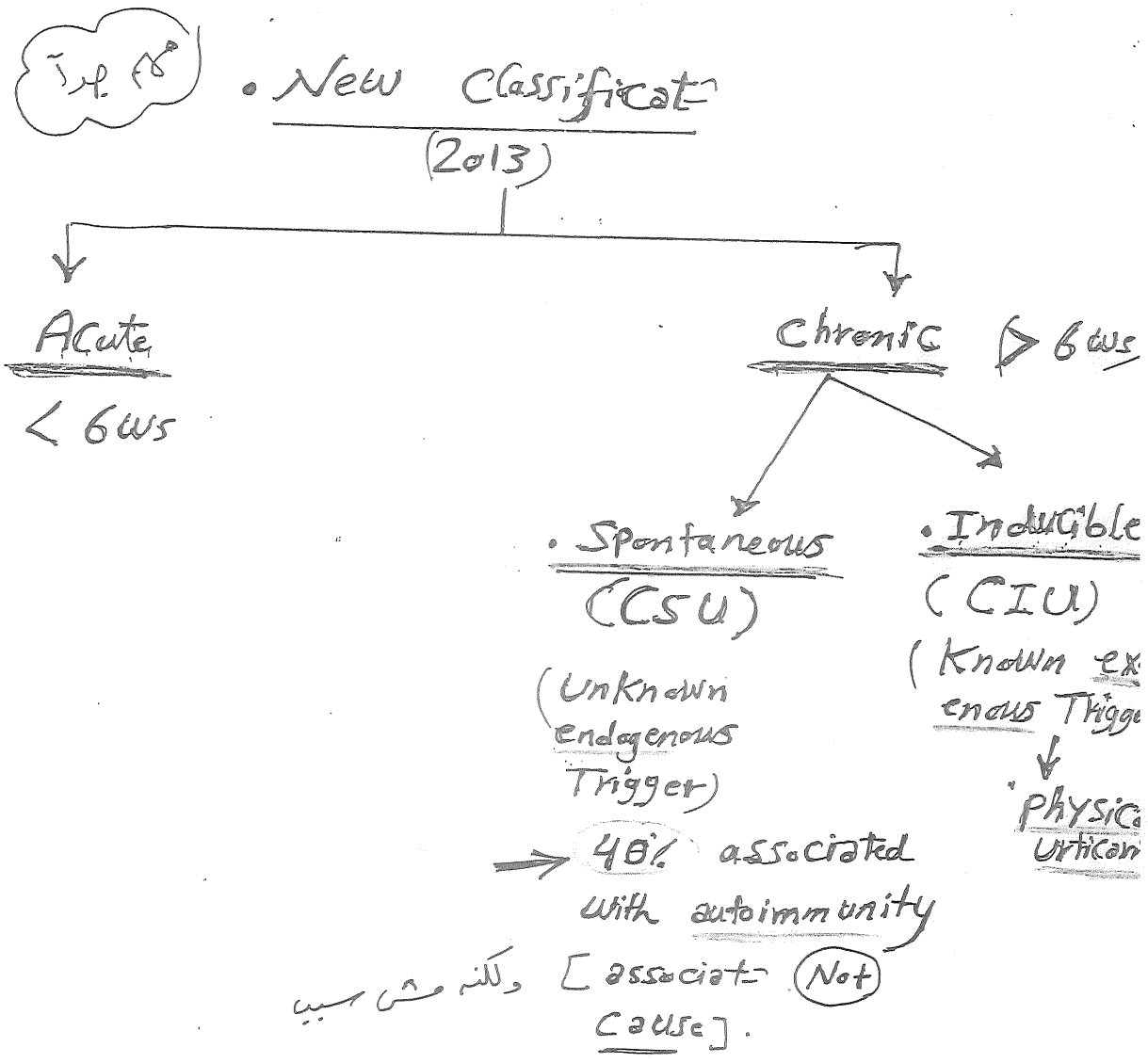
IgE Mediated urticaria (Hence Transmitted by serum)

3
- Cold urticaria
- Dermatographism.
- Solar

Classificat Urticaria

(Weals)

- < 2 hrs
  - Physical Urticaria
  - Except ??
- 2 - 24 hr (Evanescent Confirmed by: Circle test)
  - Ordinary Urticaria
    - Course of dis.
      - < 6 Ws: Acute urticaria
      - > 6 W
        - < 2 unit/w: Episodic Urticaria
        - ≥ 2/w: Chr. urit U
- > 24 hr (إذا Biopsy)
  - Urticarial Like Rash
  - إذا U. Vasculitis
  - urticarial EM
  - prodroma of BP
  - Eosinophilic Cellulitis
  - Drug Erupt
  - Viral Exanthema
  - Insect bite
  - AHEI


• New Classificat
(2013)
Acute
< 6 ws
Chronic > 6 ws
• Spontaneous
(CSU)
(Unknown
Endogenous
Trigger)
40% associated
with autoimmunity
[associat Not
cause].
• Inducible
(CIU)
(Known ex
enous Trigg
• Physic
Urtican

Ordinary = Spontaneous

Acute Urticaria (Acute ordinary)

Def. Recurrent Episodes of urticaria that has a course of Less than 6 Ws (< 6 Ws).

Triggers of Acute urticaria

- Summary:
  - 50% → Idiopathic
  - 50% → Known Causes:
    - 40% URT Viral Inf.
    - 9% Drugs.
    - 1% Foods.
    - Others: (Inhalants-Chemical & physical stim.)

Details:

A. Idiopathic (50%)

B. Known Causes (50%)

NB

What suggest

- Autoimmune → Newcomer Fever ↓ Constit. Symp
- Food → acute, Recurr.

1 Infection:

- Viral: URT, HBV & HCV, IMN
- Fungal ← Genital Candidiasis
- Bacterial: Strept, Helicobacter*
- Parasitic: Ascaris, Ancylostoma, Strongyloides, Filiaria
- Arthropod

2- Drugs: (Allergy type)

- Aspirin, NSAIDs
- Sulfa, Penicillins
- ACE-I, Opoids
- Polymyxin B

3 Food & Food additives (Pseudo-allergy type)

- Natural: Yeast, Salicylates*, Citric acid
- Synthetic: Azo, Sulfate, Benzoic a., Penicillin

4 Physical Stimuli

Cold, pressure, aquagenic.

5 Chemical Stimuli

Latex, ammonium persulfate (in Hair chemicals)

6 Inhalents:

Pollens, Mites, Acrolein, Cosmetics

7 IV Contrast Media

- Inject.
- Ingest.
- Inhalent.
- Inf.
- Drugs

- physical
- chemical

Chronic urticaria

Def. Recurrent Episodes of urticaria, at Least twice/week that's lasts for ≥ 6 weeks (Course of the dis.)

NB : If attack occurs < twice/week for a Course of ≥ 6 ws it is not called chr. urticaria but called Episodic or "Recurrent urticaria" (usually has identifiable Cause).

Epidemiology :

(i). Affecting ~ 1% of the population.
(ii). Represent 25% of cases of urticaria
(iii). Course (سؤال المريض: هي هاتفضل طول العمر؟)
- 50% → Resolve in: 6 months
- 40% → " 10 years
- 10% : Remains for > 10 Ys.

- Urticaria alone: has better Prognosis > Angiodema or urticaria + Angiodema. (urticaria أفضل Angiodema أسوأ urti + Angi

Classification (Recent): (تصنيف)

1- Chr. urticaria of Known Etiology (10%)
- Same Causes of Acute urticaria
- chronic Medical illness

2. chr. Idiopathic urticaria: (50%) (CIU)

3. chr. Auto Immune urticaria (40%) (CAU)

Classifica
تصنيف
1- CIU (9
2- CIU
CAU
3. تصنيف

NB Chronic Idiopathic urticaria : in the past was constituting upto (95%) (no detected cause); Recently 30-50% of cases of CIU is not idiopathic but it is an autoimmune disease

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[1] Chr. urticaria of Known AET (10%):

(a) - See Causes of Acute urticaria. → Genital Candi... is the most Common Cause in Egypt female (H. pylori)

(b) - Chr. Medical illness:

- Leukemia
- Lymphoma
- Hyperthyroidism or Hypo.
- PCRV
- Cut. dis: Mastocytosis, Bullous dis.
- C.T.Ds eg SLE.
- Cryoglobulinemia.
- Cryofibrinogenemia.
- Psychogenic (Exacerba...
- Muckle Well's Synd (UDA = urticaria, deaf..., Amyloidosis)
- Schnitzler Synd: (Consider in any Urticaria or U.V ass ē fever, pain & Arthralgia).

[2] Chr. Idiopathic urticaria: (50%) (True idiopathic)

[3] Chr. Autoimmune N: (40%)

- commonest [30%] → (1) Anti FCεRIα autoantibodies. (Receptors of IgE on mast Cells & Basophils) (IgG1&3)
- least [10%] → (2) Anti IgE autoantibodies.

CAU: usually ass. ē "Antithyroid Antibodies" (Antithyroglob. & Microsomal)
& (±) Ass. ē Other Autoimmune dis. e.g.

- CTDs
- Arthritis
- Vitiligo.
- pernicious anemia.

(4) Evaluation of a case of Chr. urticaria

All Patients

1. History.
2. Examination
3. Provocative tests for physical urticaria.

Selected Patients

(severe cases not Responding to antihistamines).

- Biopsy
- XR: Chest, Sinus, Teeth.
- CBC
- ESR
- Urine analysis
- Stool analysis
- Hepatitis B & C
- Antithyroid AntAbs (2)
- ANA
- Cryoproteins
- Tests for IgE.

Chronic autoimmune urticaria:

Note: Autoimmune and non-autoimmune cases are indistinguishable clinically and histologically but the following features may raise the sucipision of autoimmune type:

1. Tend to run a more aggressive, treatment-resistant course (to histamines)
2. +Ve Antithyroid antibodies.
3. Female
4. History of other autoimmune disease (personal or family H.)
5. worsening during the monthly cycle (women only)
6. Past history of remission or remission during pregnancy

Diagnosis of autoimmune urticaria:

1- In vivo test: **Autologous serum skin test (ASST)**

* Indicated only in patients with chronic ordinary urticaria who are poorly responsive to routine treatment

* All H1 antihistamine treatment should be withdrawn at least 48h prior to the test (2 weeks for systemic steroids).

* Serum is obtained from the patient during a period of disease activity and 0.05ml is injected intradermally into the forearm skin on both sides. Similar control injections of saline and histamine (10µg/mL-1) are performed

* A positive result, read at 30 min, is a red wheal at the serum sites of diameter>1.5mm greater than the saline wheals

* **Significance of a negative ASST**: essentially rules out autoimmune urticaria. [Good -Ve test]

* **Significance of a positive ASST**: indicates the presence of autoreactivity in the serum, but in- vitro confirmation is required before this can be identified as due to functional autoantibodies.

* The ASST has a sensitivity of 70% and a specificity of 80% (IJDVL) 2010

2- In Vitro Basophil Release Assay test: to Confirm +Ve ASST. (only for research)

(أكاس) **physical urticaria** 8

- urticaria caused by physical stimuli
- (20%) of all types of urticaria.
- Commonest types "بالترتيب"
  - ✓. dermatographisme
  - ✓. cholinergic
  - ✓. cold
  - ✓. pressure. →

NB
- lesions lasts for <2hrs
  Except:
  1. Delayed presure U.
  2. Familial cold
  3. Delayed dermatograph

- Types
  1. Dermatographism
  2. cholinergic → (أكاس)
  3. Adrenergic
  4. Cold
  5. Heat
  6. vibratory
  7. Galvanic
  8. Aquagenic
  9. Exercise induced
  10. Solar.
  11. pressure.
  12. Contact U.

Dermatographism (Dermographism) (skin writing)

Exaggerated Triple Response of Lewis → (تكونا) :-

- (E) ① Flush (Erythema) → d.t capillary VD
- (F) ② Flare (brodening Erythema) → local Axon Reflex. ← ass ē mild itching
- (W) ③ Wheal → d.t Transudation [oedema] (arteriolar VD)

this response can be Elicited by:
stroking blunt > ① skin stroking by blunt object (Not rubbing)
② Histamine Inject

Normal → The Triple Response of Lewis is aNL skin response To stroking by blunt object or Histamine InJ. (if) this response is Exaggerate → (Severe reaction + Severe Itching) → It is called "Dermatographism"

- Icid: 10% of general populat

Types of Dermatographism

- **True dermatographism:**
  1. Immediate (classic)
  2. Delayed (less common)

- **False dermatographism** (misnomer's Not ass with Urticaria).
  - Black
  - White
  - Red
  - Yellow

  عل مصر (Black, White)

Immediate (Classical) Dermatographism

NB. other Types — follicular, cholinergic

Triggers → **Dermatographism** linear or Irreg. Wheeling & Itching of sites of Trauma, Cloth friction & skin scratching
[لو بيهزر مع مراهبة ومسكة مترولعة]

Triggers:
- Spontaneous (++)
- or following: (+)
  - inf
  - stress
  - Drugs
  - Helicobacter
  - Scabies

- AEtiology → Ig E Mediated (So Can be Transmitted by Serum)
- prognosis → unpredictable. مش نعرف ها تخف امتى

Delayed Dermatographism:

stroking → No Reaction or Immediate Dermatog. (ع كيفي) → 3-6 hrs (دايم 30 min.) → occurance of Dermatograph or Recurrence of Dermatog.

at same site that may last ≃ 48hrs

False Dermatographism differs from True in:

1. Red — Induced by rubbing (Not stroking). ass. ē SD
2. Black: discoloration by pressure ē Metalic object.
3. White: Light pressure → Blanching (Capillary VC)
4. Yellow: bile pigment deposits.

(عفوي) → 2, 3: حدث ع / حكه — Atopy, M.F, DS.

Ttt → Antihistamines (specially Hydroxyzine) or phototherapy.

(أكثر) Cholinergic urticaria (5%) (induced by Acetyl choline → ++ Mast Cell → Histamine)

• Triggers:
- Emotional stress
- Exercise
- ↑ Enviromental Temp (الجو الحار / الغذاء الحار)
- Spicy food

→ ↑ Core Body Temp (15 mins) → Acetyl choline Realse → ++ Mast Cells → Cholinergic urticaria

• Cholinergic urticaria ± manifested by: either:

① Minute (2-3 mm), Punctate, highly pruritic wheals or papules that may effect whole body Except Palm, sole, axillae & Surr. BY "Flare"

or ② Just: Itching, prickling & Burning Sensation (cholinergic pruritus) → Each attack usually followed by Refractory period of ≃ 24 hrs.

NB: systemic symptoms ē Anaphylaxis ± occur.

التشخيص:
Provocative Tests (استفزازية):
- Excercise
- Warm bath
- Methcholine test

Best → Atarax

##:
① أول ما يحس: حمام سخن أو مجهود عشان Attack → Refractory period
② حمام بارد أثناء الـ Attack
③ Zyrtec + Atarax "أهم"
④ Zaditen (30-150 mg/d)
⑤ Inderal BB (in patients ē isolated induced Exercise or Anxiety)
⑥ DanaZol (Severe Cases)
⑦ Anticholinergic.

• Adrenergic Urticaria

Triggers:
- Emotional Stress
- Exercise
- Coffee
- Chocolate

→ ↑ Serum Catecholamines (Epinephrine, Nor ") → Attack: lesions similar to Cholinergic but Surrounded By Pale Halo

Provocative test: 3-10 ng Epinephrine inj.

##: ① Propranolol ② Atenolol } BB

Cold urticaria

- urticaria Induced by cold exposure
→ doesn't develop during "chilling" but on Rewarming
- usually affect the face & Hands (ACtal)

3 Types

1ry (Essential = Cold u.)

- (Not) associated ē any underlying systemic dis.
- usually begins at adulthood
- Clp:
  1. Wheals at site of cold Exposure (for mins)
  2. Cardiovascular collapse & fatal shock if swimming in Cold Water (... ينزل الماء عوت)

Provocative Ice Cube test → +ve. (للتشخيص)
- 5-20 min → then fanning For additional 10 min. → React.
- not done if 2ry Cold urticaria is Considered → don't do the test as it may Cause Vascular occlusion & tissue ischemia.

2ry

- Associated underlying diseases
  - Cryoglobulinemia
  - Cryofibrinogenemia
  - Hepatitis.
  - Hemolysins = (2ry ✗)
  - IMN.

Familial

- +ve F.HX
- Grouped recently
- Autoinflamm. syndromes.
- Ch° By:
  - durat°: 1-2o
  - Burning > itch
  - cyanotic center
  - surr. by pale Halo.
  - → Ass. ē leukocytosis

Reflex Cold

Ice Cube -ve but at Room 9°C → Rash

Treatment

Triactin ... Best

A. Instructions

1. Avoid Sudden ↓↓ in Body Temp.
2. Aquatic activity should be done under supervision.
3. ↑↑ of underlying etiology e.g Cryoglob.

B. Drugs

- Triactin (cyproheptadin)
- Doxepin
- Ketotifen
- others Cs, CyA

Heat urticaria: may be: (Heat > 43°C for ≥ 5 min) → 2 Type of react:

- **Localized React:** (at site of Heat applicat)
- **Generalized:** may be acc by:
  - Cramps.
  - Weakness.
  - Flushing.
  - Salivat.
  - Collapse.

- **Provocative test:** Heat Cylinder (50 °C) applied to skin for 30 mins → Reaction.

- **Vibratory urticaria:**
  - Vibration:
    1. Body toweling
    2. Tooth brush.
    3. occupational (drilling)
    4. السيشوار

    → React ± تزا سكل ← dermatographism, cholinergic, pressure.

- **Galvanic urticaria:** (Iontophoresis) d.t exposure to galvanic device during ttt of (Hyperhidrosis)

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* **Pressure (delayed pressure) urticaria:** (مهم جدا جدا)

- Severe sustained pressure after Interval usually (3 - 6 hrs) (less Common 12-24) → Reaction

  e.g
  1. Feet: prolonged < Standing & Walking
  2. buttocks: Prolonged sitting
  3. straps of < Bra. / أستك بنطلون. / أستك شراب.
  4. شنطة < ساعة

"مهمة جدا"

متحصل بعد ٣-٦ ساعات وبتقعد اكتر من: ٢٤ ساعة

- Reaction:
  - Edema (Wheal): lasts for (8 - 72 hrs)
  - Pain
  - Others < Fever. / Chills. / Arthralgia. / leukocytosis

- **Provocative Test:**
  - 15 pounds Hanged to Hands For (20) mins then → "Observe for Reaction"

    (Pound = 1/2 kg)

  تشيل ١٠ kg

NB

immediate pressure urticaria is rare idiopathic disorder that has been described in patient c Hypereosinophilic synd.

Treatment

- Cs ← Topical / Systemic : ↓ itching & pain (Controversy)
- NSAIDs
- Antihistaminics
- IVIG

Solar urticaria

DD → PML: onset & resolution (1-4 d)

Visible light & UVL → Few mins → Wheal, Erythema & React → Clear ein (1 hr) (+)

- May be transmitted passively (so, thought to be IgE induced)
- ttt
  - avoid UVL by sunblock
  - $H_1 + H_2$
  - * desensitization

2 Types:
- 1ry: IgE Mediated ag cut or circulating irradiation induced Ag
- 2ry: → in porphyria.

Exercise Induced urticaria

Note: Both Cholinergic & Exercise induced urticaria ppt BY: Exercise So How to diff. ??

1. ↑ Core body temp doesn't ppt Exercise induced
2. Larger Wheals than those of cholinergic (tiny) ← NL size urticaria (Wheals)
3. (Delayed) Wheals appear (5-30 min) after Exercise.
4. Usually Complex Synd. ← pruritis, urticaria, angioedema, syncope

ttt:
- $H_1 + H_2$ blockers
- Self injected epin. Kits for those develop Anaphylaxis

Aquagenic urticaria

Triggers:
- Water (at any temp.)
  - sweat
  - saliva
  - Tears

Immediate or ein few mins → pruritic Wheal ± systemic manifs

Water is direct Urticariogenic

AET: Unknown, ± d.t
Water Sol. Ags → diffuse into dermis → Histamine Release

Treatment

(2P)

1. Petrolatum film to body → prevent it
2. Antihistamines → Effective (قبل الاستحمام)
3. PUVA → prevent skin lesions (Not) pruritus.

urticarias & pruritus Related to Water

(المشاكل المتعلقة بالماء)

1. only ē Cold Water → Cold urticaria
2. " " Hot Water → Heat u. or → cholinergic urticaria.
3. urticaria with (any) Water Temp → Aquagenic urticaria
4. pruritus (with) any Water Temp. (No lesions only itching) → Aquagenic Pruritus

immediate or ē in few minutes of contact or following cessation of water

[أولها جسمه يلمس الماء أو بعدها بثوية أو بعدها يخرج من الحمام بثوية صغيرة]

↓

Pruritus or prickling or Burning sensation (هرش / حرقان / شكشكة)

(طرقة مطول ١٠-٤٠ دقيقة)

↓

Investigate Before ℞

1. (+ve) FH
2. PCRV
3. Myeloprolif. & Myelodysplastic synds
4. Hypereosinophilic synds
5. Juvenile XG
6. Xerosis of old age.

℞ (Aquagenic Pruritus)

- Antihistamines
- Propranolol (Inderal)
- Na bicarbonate → (تضاف للماء الحمام)
- Phototherapy.

- NBs

- Anaphylaxis ttt

① Cardiac & Respiratory support

② Epinephrine: . diluted 1/1000 → give 0.3 mL every 10-20 mins.

. children: dilute 1/2000.

③ Adjuvant ttt: . IM anti-Histamines 6hrs (Hydroxyzine or diphenhydramine)

. Cs: 250 mg / 6hrs Hydrocort.
50 mg / 6hrs MPA.

- Auto inflammatory Synds.

** inherited disorders ch' By

1- inflamm (bouts)
2- Fever (periodic)
3- Rash.

bouts of inflamm. | periodic fevers

(+) prominent cut. manifs p.
- Acne
- PG
- erysipelas
- urticaria like rash.

include

① FMF (AD)
- fever
- serositis
- Arthritis
- Erysipelas like rash

→ ttt 1- Colchicine
2- Thalidemide (in Colchicine resistant cases)
3- Herbal Remedies → Sc affection

② PAPA Synd (AD)
- Pyogenic arthritis
- PG
- Acne.

③ TRAPs (TNF receptor Periodic Synd): Similar to FMF but differ in
- longer attack
- not respond to Colchicine.

④ Familial Cold urticaria

⑤ Muckel Wells Synd:

. acute, febrile, inflammatory episodes;

Comprising
- Abd. Pain
- Arthritis
- Urticaria
- amyloidosis

(3A)

Treatment of Urticaria

(A.) General Lines (Non drug therapy):

1. Avoidance of possible triggers:-

- Drugs: avoid aspirin, NSAIDs
- Diet: " Food coloring & preservatives (salicylates) — low pseudoallergen diet.
- Avoid: stress, overheating (تقفيل تكييف) & Alcohol.

2. Cooling lot's: (Calamine & 1% Menthol in aqueous cream).

(B) Drug therapy: 3 lines

كفك جيد آجيد

First line:
Modern second-generation antihistamines

↓ If symptoms persist after 2 Weeks

Second line:
Increase dosage up to fourfold of modern second-generation antihistamines (أزودها لحد ٤ مرات)

↓ If symptoms persist after 1-4 further Weeks

(3rd line)
- Add to 2nd line: omalizumab or / ciclosporin or / Montelukast
- Short courses of systemic Cs (<10ds) only during exacerbat.

Some second-line medications for chronic or physical urticaria.

Generic name	Dose	Special indication/associated diseases
Prednisone	0.5 mg/kg qd	Severe exacerbations (days only) ١٠ أيام
Epinephrine	300–500 mg →	Angioedema of throat/anaphylaxis
Montelukast (مريض قلب بياخد اسبرين)	10 mg qd	Aspirin-sensitive urticaria
Thyroxine	50–150 mg qd	Autoimmune thyroid disease
Nifedipine (مريض ارتفاع ضغط عالي)	10–40 mg modified-release qd	Hypertension
Colchicine Dapsone	0.6–1.8 mg qd 50 mg X2	Neutrophilic infiltrates in lesional biopsy specimens
Sulfasalazine	2–4 g qd	Delayed pressure urticaria

Urticarial Synds:

1. Schnitzler synd.
2. Muckle-Wells ← Amyloidosis, deafness, urticaria

AUD عود

(3) • Capillary leak Synd = (Clarksons synd)

← انفصال Endoth Cells لمدة أيام : ظاهرة غريب .

ضخ fluid ↓

- ✓ - Leakage of fluids
- ✓ - HypoTN
- ✓ - HemoConC.
- ✓ - Hypoalbumin
- ✓ - Edema
- ✓ - Monoclonal IgG.

Drug Induced (IL2)

(4) Autoinflammatory Synd

- Familial Cold
- FMF
- PAPA
- TRAPS

Angiodema.

Acute, circumscribed oedema that affect → skin & MM.

→ differs from urticaria in:

① site of lesion / oedema:
- lesion:
  - skin: of most distensable areas as
    - Eyelids
    - Lips
    - Earlobes
    - Genitalia.
    - also may affect others → diffuse swelling of → Hands, Feet, forearms.
  - MM → R.T → asthma & Asphyxia; GIT → Abd. pain.
- oedema → S.C.T & deep dermis (urticaria = dermal only)

مقارنة سريعة

Urticaria.	Angiodema.
Wheals	oedema
superfacial Dermis	deep dermis & S.C.T
Pruritus +	No
Pain: NO	+
Site: only skin	distensable skin & MM
Duration: <24 hrs	48-72 hrs.

ملاحظة [urticaria affect non distensible]

② usually ass. ē Pain Rather than pruritus;

Classification of Angiodema

- Associated with Wheal / Pruritus → Considered as a case of urticaria
- Not ass. with Wheal / pruritus → Classification 6 (Clarkson synd):
  - Idiopathic non Histaminergic Angioed. (INAE) → Tranexamic acid.
  - C1 esterase inhibiter defect → Hereditary / Acquired
  - Episodic Angiodema ē Eosinophilia (Gleish synd)
    1. Fever
    2. W.t gain (↑)
    3. Eosinophilia (↑)
    4. Episodic angiodema
    5. مهم → (↑) IL5 during attack.
  - Drug induced → ACE inhibitors (ACEI) & NSAIDs → -- Kininase enz. → ↑ Kinins.
  - Oestrogen-dependant

Eostrogen depend. مهم جدًا
Now d+ factor XIIa Mutat. → ↑ Kinins.
Hagmen Factor

Hereditary Angioedema (HAE)

(Quinke edema)

(Hereditary C1est. Inhibitor deficiency)

- AD
- Age: 1st & 2nd decades
  - 4ai. < 5 Ys
  - 75% at 15 Ys.
- +ve FH.

*There may be a Trigger of:

1. Minor Trauma
2. Surgery
3. Emotional stress
4. change in temp.
5. estrogens in (OCPs)

→ Sudden attack of Angioedema (ch` By:

- Every: 2 Weeks
- Lasts for 2-5ds

X · No Urticaria or pruritus

- 0-2a Ys
- 12 Ws
- 2-5 ds

3 Common Sites

Skin

- Face
- Hands
- arms
- Legs

Acral

- buttocks &
- genitalia.

GIT (±Renal)

- stomach
- Intestine
- Bladder
- Kidney

- Vomiting
- diarrhea
- Pain (± Acute)

Respiratory Tract

- Laryngeal oedema
- air way obst. & Asphyxia.

- pathophysiology → See before

- deficient C1-INH → Excessive activat of C2 & C4 → ↑ Kinins → ↑ Vascular permeability → Angioedema.

C1 esterase Inhibitor
(C1-INH)

(Physiology) • Classical pathway of Complement

لبداية Ag + Ig < G or M → Ab

↓

C1 activat (has 3 subunits)

- C1q (largest subunit bind to Fc part of Ig).
- C1r —++→ C1s
- C1s (so after its activat it Acquire Esterase Activity so called (C1-esterase enz))

C1s → ++ C4 → ++ C2 → C3 Activat → Kinins —VD→ Angioedema

Kinins ↑ Kininaseenz. ← (ACEI) → destruct

(F) ... :
1- Fibrinolytic
2- clotting
3- Kinin
4- Factor XIIa

(physiologically): this pathway is Controlled (inhibited) by enzyme that — C1 esterase

So Called : (C1 esterase enz inhibitor)

. Any defect in this enz ⟶ failure of control & regulat of this pathway → ↑↑ Kinins → Angioed.

(NB) **Deficiency of C1 esterase Enz inhibitor**

(±)

- Hereditary (+ FH) (<20 Ys)
- Acquired (−ve FH) >40 Ys.

• There are 2 Types of Hereditary C1EI deficiency Angiodema.

Type I (quantitative defect)
- there is ↓ level of (C1-EI)

Type II (Qualitative defect)
- there is (NL) or (↑↑) level of C1-EI but it is dysfunctioning.

• To diagnose type I & II

• أول حاجة نقارن:

• C4 & C2
(level usually < 40% of NL d.t continous activat. & consumption)

• If ↓ C2 & C4.

↓

C1-INH assesment <
- Type I: ↓↓ level
- Type II: NL or ↑↑ but dysfunctioning.

• Note <
- C4: ↓↓ during & inbetween attacks.
- C2: ↓↓ during attacks only

[Sodo (C4) assesment] ← أفضل

Treatment of HAE (updated 2012)

Acute attacks

1. C1E-INH replacement (Not for Type II)
2. ICatibant (bradykinin B2 Rs antagonist)
3. ECallantide (kallikrein --)

↓ alternative

Fresh frozen plasma

وقتي
* Maintain airway
* Tracheostomy if Needed.

Inbetween attack

- Short term prophylaxis (Before Endoscopy or Minor surgery)
  - Danazol (600 mg) ٥ أيام قبل وبعد العملية
  - C1-INH ساعة قبل العملية
- Long Term prophylaxis
  - Danazol (200 mg/d)
  - Antifibrinolytics
    - Tranexamic acid (TA) (كابروك)
    - Epsilon amino-caproic

Anti-Hge Agent

- NB:
  - FDA: C1-INH (Ruconest)®
  - Danazol: مع الأطفال
    - 17-α Alkylated androgens.
    - SE 1- Hepatotoxic & Hepatocarcinogenesis (rare) ← يسبب سرطان الكبد
      2. HTN (↑)
      3. Hyperlipidemia
      4. Virilization of ♀ if during pregnancy (تذكير الجنين)
    - CI ① Cancer prostate
      ② Pregnancy & Breast feeding
      ③ Childhood

Acquired C1-EI deficiency

- Same C/p as HAE but differin (onset > 40 ys / No FH)
- there are 3 Types

• Type I (Well synd)
- Consupt Abs.
- rare
- d.t Overconsumpt of C1-EI & C1 (↑ Catabolism) d.t ↑ product of Idiotypic Igs → Ag/Ab Complexes ē Comp Activat
- Ass. with:
  - Myeloprolif. disorders (leuk, Lymph. carcin. MM) (BCL ؟؟)
  - SLE & APS
  - Vasculitis (Churg Strauss) & Cryoglob.
  - Viral inf. HIV, Parvovirus B19.

• Type II
- Blocking Abs
- Extremely rare
- d.t Antibodies directed against C1-EI → Blocks its funct
- No ass. diseases.

• Type III (Idiopathic)

In Both Types
- ↓ C2 & C4
- ↓ C1-INH
- Type II: +ve Immuno Blot test for 95kd- e- INH cleavage product
- ↓ C1q (الفرق عن الـ HAE)

⊕ Type I: As HAE

⊕ Type II → Immunosuppressives: Cs, plasmapheresis. (No danazol)

(aq) . Estrogen dependant Angiodema : this type ch` By

Hagema factor (فاكتور جديد) XIIa Mutat (this factor: ↑ly → ↑ Kinins)

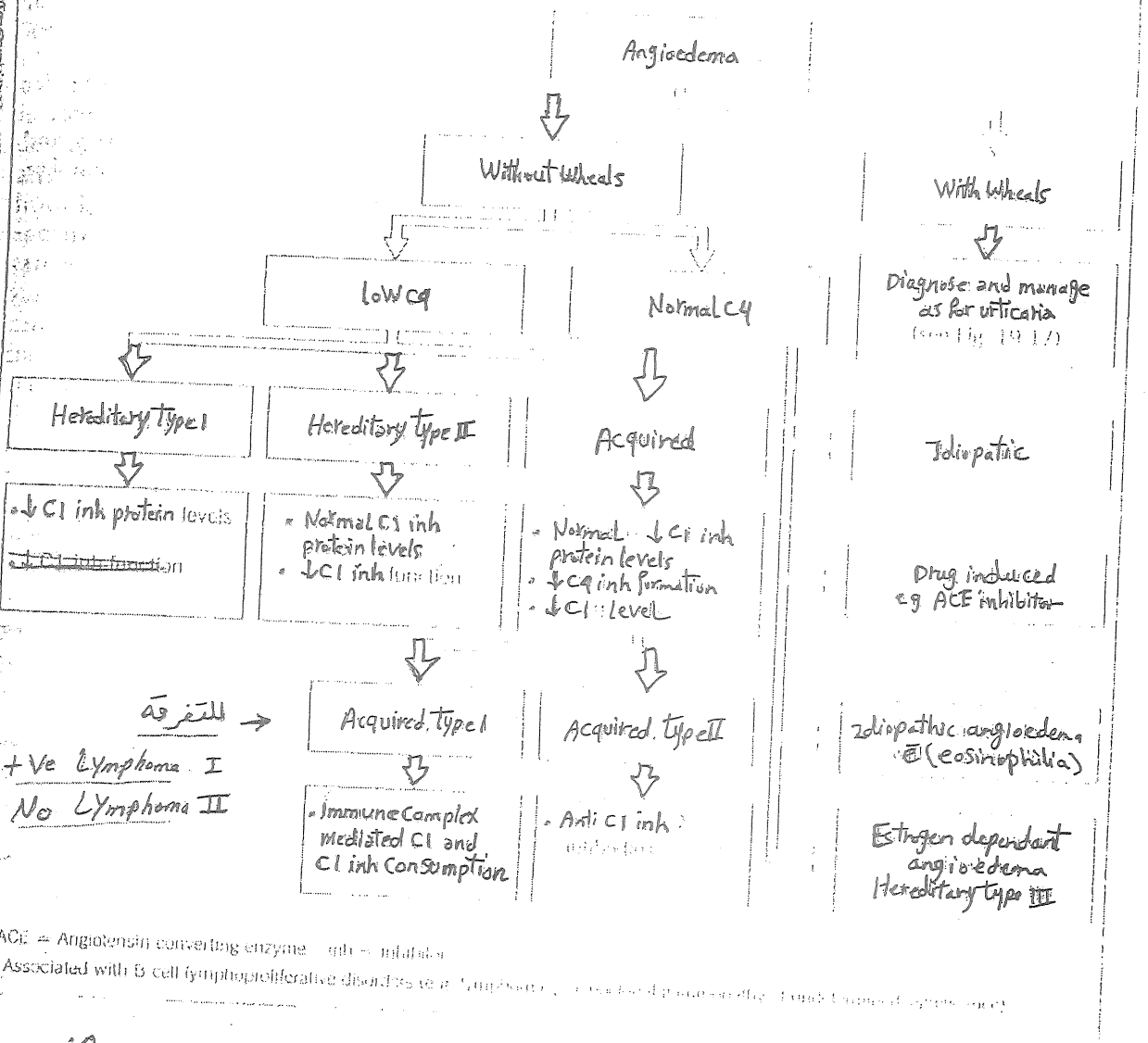
1. Hereditary (+Ve FH)
2. NL C1-EI & C4.
3. Failed response to Cs, C1EI replacement. (but to Danazol or Kallikrein inhibitors)
4. unknown Mechanism. but ± d.t upregulat of Kinins (by) Estrogen.

لو عندك اختيار: Hereditary Angiodema → C1-EI defect. (Type I & II) / Estrogen dependant (Type III)

NB . HAE may be overlaped ē Auto-inflammatory Synds.

. Oestrogen dependant Angiod: is hereditary but not d.t C1 esterase inhibitor defect.

ALGORITHM FOR THE DIAGNOSIS OF ANGIOEDEMA



diff. bet. Urticaria & Urticarial Vasculitis:

- Urticaria & Vasculitis.
  - ⊙ Lesions (Wheals) Lasts > 24 hrs
  - ⊙ Pain Rather than Pruritus
  - ⊙ Resolve ē Post inflamm. Hyperpigm
  - ⊙ path. → Leukocytoclastic Vasculitis.

Antihistamines

(أنتي)

Ref.
- Emad
- Blogania
- Comprehensive
- other Sources

- Mechanism: Inverse agonist rather than antagonist (Competitive)
  ↓
  bind to histamine R_1 → ↓ its activity below its constitutive activity (down regulation the constitutive activated state of corresponding Rs).

- Types of Histamine Rs:

- H_1 Rs: 3
  ↓
  - VD & ↑ permeability of BVs → Erythema & Edema (Weal)
  - Axon reflex → Flare & Itching
  - ± other Smooth ms → Contract → Bronchospasm

- H_2 Rs: 3
  ↓
  - VD & ↑ permeability
  - ↑ Gasteric acidity
  - others: Immunomodulating act (T cell down-regulate)

  → [So H_2 blockers → Used for ↑↑ Inf. ass ē Impaired T cells e.g.
  - CMC
  - Warts]

- H_3 (auto Rs) — inhibit for 2
  (i) -Ve feedback on histamine Biosynth.
  (ii) Inhibitory Neuro-Transmitter in brain (-- SR, Norepin & ACh)

- H_4
  - Expressed on Human dermal Mast Cells, Basophils & Macrophages.
  - Funct → "Mediate Mast Cell Chemotaxis"

(B) - In Urticaria: - Itching: Mediated by (H1 Rs)
- Edema & Erythema: Mediated by both (H1) (H2) (H2 > H1)

(↑↑S) (So Anti-H2 has little effect in ↑↑ of Urticaria).

• Classifications — Anti H1, Anti H2, TCA, Mast cell Stabilizers.

(A) Anti H1 Antihistamines:

Class	Examples	TRADE	Daily adult dose[1]
Classic (sedating)	Chlorpheniramine	· Analletge · Avil	4 mg tid (up to 12 mg at night)
	Hydroxyzine	→ Atarax 10mg	10–25 mg tid (up to 75 mg at night)
	Diphenhydramine		10–25 mg at night
	Doxepin[1][2]		10–50 mg at night
Second-generation (Low or Non Sedating)	Acrivastine	· Semprex	8 mg tid
	Cetirizine	· Zyrtec	10 mg once daily
	Loratadine	· Claritine	10 mg once daily
	Mizolastine		10 mg once daily
Newer second-generation	Desloratadine	· Aeriius · Desa-5	5 mg once daily
	Fexofenadine	· Telfast 120/180	180 mg once daily
	Levocetirizine	· Levocet	5 mg once daily

- Fenistil® → Dimethindine
- Evastine® → Ebastine (10mg)
- Triactin® → Cyproheptadine (anti H1 Serotonin) → SE: ↑ appetite → ↑ wt; GR (in children)
- Tavegy® → "Climastine" 1mg

(B) Anti-H2 (H2-Blockers):

- In skin Histaminic Receptors are: 20% H2, 80% H1
- Anti H2 are: lower efficacy, lower significance
- Should(n't) be used alone in cases of urticaria as Without Anti H1 → Exacerbation
- Examples:
  - Famotidine, Ranitidine (150mg X2/d)
  - Cimetidine (400mg X2/d)
- S.E: GIT upset, Hair loss, Antiandrogenic (Cimetidine)

(C) Tricyclic Antihistamines :→ Doxepin — Very strong anti H_1 & H_2; Strong: 5HT & α adreng inhibitor

(D) Mast Cell stabilizers:

- Cromolyn Na (Inhalation)
- Ketotifen (2nd generation Anti H_1 & Mast Cell stabilizers).
  ↓
  Main use: physical urticaria. / Urticaria Pigmentosa. (متورط طفح)

Pharmacokinetics:

- Metabolism: BY hepatic CYP450 → طبعا عرف Interact
- Excret: all renal Except: (Little renal EXC). (DLD)
  - Diphenhydramine
  - Loratadine
  - Desloratadine.
- Plasma Peak Conc ē in 1-2 hrs; So its benefit appears ē in 1-2 hrs So not used at or after onset of urticaria [should be given as a preventative rather than on an as required basis].
- Half life. Longest: 1st class: Chlorpheniramine; 2nd gen.: Desloratadine.

NB:

- Hydroxyzine → Metabolized to Cetirizine → Levocet.
- Loratadine Metab to Desloratadine. (14-34)

(S.E)

. 1 Generation has 2 main S.E: بتقل بعد سوبيس شعرا ضرح

(1) Sedation d.t lipophilic → Cross BBB → Sedation but Hyperexcitability & Seizures may occur specially ē large doses in (children). also → Impaired Cognition → ↑ apetite

2nd generation
. No or little Sedation
. No - anti-cholinergic S.E.

(2) Anticholinergic S.E (Atropine like acts) → Anticholinergic Synd:
. Xerosis < skin, MM
. urine retention & Constipation
. Tachycardia
. dilated pupils
أهم [. ED. . Glaucoma.

!! .. أخطر الشاكل
. Urine Retention (BPH ē)
. Glaucoma

Drug Interactions: (All ē drugs that interact ē (P450).

. Terfenadine
. Astimazole

→ if taken ē CYP450 Inhibitors as . Ketoconazole . ErythromyCin . Cyclosporine . Cimetidine . Nafedipine. → Cardiac arrythmia & death. (علشان كده اتشالوا من السوق)

Uses of Antihistamines:

. Insect bites
. Urticaria & Angioedema
. Urticaria Pigmentosa.
. Pruritus
. Others.
  . Sedation before operation
  . ↓ Nasal stuffness in Hay Fever & during Cold.
  . Counteract Motion Sickness
  . ↑ apetite.

. pregnancy
. Lactat
. Hepatic
. Renal

Clinically important Points to be considered

Pregnancy

1- Sedating antihitamines: all category (B) except hydroxyzine and doxepine (C).

1- Non-Sedating antihitamines: cetrizine, levocetrizine and loratadine category (B) while fexofenadine and desloratadine (C)

Nevertheless, a first-generation antihistamine, such as chlorpheniramine, may be considered the drug of choice because the cumulative experience of use of this agent in pregnant women is greater

(دي الخلاصة بقي في الحمل...وافضل نوع مع الحمل علي الاطلاق هو كلورفنيرامين)

Lactation:

كلهم لا ينصح استخدامهم اثناء الرضاعة. Caution in nursing.

· if Sedating given in Lactat → Insomnia seizures & agitation if Neonate → Stop.

Children: age of approval is: Cetirizine and fexofenadine ≥6 months- Desloratadine ≥1 year- Loratadine: ≥2 years- Levocetirizine ≥6 years- Hydroxyzine has been used to alleviate pruritus in children with atopic dermatitis and is an appropriate second-line agent in children with chronic urticaria refractory to low-sedating antihistamines.

≥6m. ≥6y. ≥1 ≥2.

Kidney or liver impairment

For cetirizine, 60% is eliminated via the kidneys. For levocetirizine, the figure is 85%. Most H1 or H2 antihistamines undergo presystemic metabolism in the liver via cytochrome P-450. *A reduction in dose of low-sedating antihistamines is advised in patients with liver or renal failure.*

(افضل حاجة في مريض الكبد *fexofenadine*)

Efficacy:

1- *According to the potency :* (1) levocetirizine, (2) cetirizine, (3) fexofenadine, and (4) loratadine.

2- *Hydroxyzine* is the drug of choice for treatment of dermographism and cholinergic urticaria. *Cyproheptadine* has both antihistamine and antiserotonin activity and may be the most effective for "cold urticaria."

سؤال امتحان ○ Malizumab (Xolair)®

Def. Humanized Monoclonal Antibody (IgG) x that binds To Free Circulating IgE (binds to Cε 3D domain of IgE).

· also ↓ FCεRI on Mast Cells, Basophils, Monocytes.

· Indications

(I) FDA (2013) → Asthma in Pts > 12y. & CSU (2014)

(II) Non FDA

Not responding to H1 blocker Pt > 12y

. AD
. BP.

· S.Es

(1) Anaphylaxis (مادة حافظة)

. 1-2 / 1000 case
. Not d.t Polysorbate but d.t protein already. Nature of Drug (as the patients are allergic)

. بعد حقن لازم يقعد المريض بالعيادة ٣٠ دقيقة ساعتين وتكون محضر كل حاجة عشان لو حصل Anaphylaxis

(2) Stroke
(3) Heart dis.
(4) Headache & Earache
(5) Inject. site react.
(6) Musculoskeletal Manifestations

· Dose: SC 150 - 300 mg / 2-4 wks

حقنة أو حقنتين كل شهر

(Ampoule = 150 mg)

Topical Corticosteriods

Mechanism

1- Antinflammatory

2- Antiproliferative: ↓ DNA synthesis specifically → Lympho & Fibrob
→ ↓↓ Collagen → Atrophy
[all Cs Have these effect except → Hydrocs sone, Dermato

3- Immunosuppressives: -- → CMI: ↓ IL2,3,4,5,6 → ↓ T cell prolif.
HI: ↓ IFN-γ
↓↓ Igs product.

4- Vasoconstrict (VC): ↓ → Erythema, Edema, Heat [& ++ of Hemangioma]

[5. Glucocorticoid Activity
[6. Mineralo Corticoid Activity

NB → Antinflammatory effect is d.t binding to 2 Types of Rs

- CM Rs
  - CM disrupt
  - -- phagocytosis & lysosomal release.
- Cytoplasmic Rs

[A] · Cs + Cytosol → enter the nucleus → interact ē Nuclear DNA → product of steriod induced proteins ((Lipocortins))
→ (--) Phospholipase A2
→ (--) Arachidonic acid formation
→ (↓) synth of → PGs, leukotrienes, PAF.

[B] -- COX enzyme.

• Classificat° According To Potency

I. European: ٤ درجات وهى الاصل

II. American: (مبيعا) ٧ درجات → Classes

- I superp…
- II potent
- III potent
- IV midstr…
- V midstr…
- VI mild p…
- VII least potent

• European classificat°

احفظوا زي اسمك

(كفاية جيداً عشان الشغل بالتجربة و شكل السوق)

1. Mild Potent (Antinflammatory activity; 1-10)

- Hydrocortisone (Micort)® (Hydrocortisone)®
- آكلوميثازون . Aclomethasone (Perderm)®

2. Moderate Potent (Antinflammatory " 10-100)

- كلوبيتازون . Clobetasone butyrate (Eumorate)®
- Hydrocortisone in Urea 1%

3. Potent (Activity 100-500)

- Betamethasone
  - Valerate 0.1% (Betaderm)®
  - dipropionate 0.05% (Diprosone)®
- Mometasone (Elocon)®
- فلوتيكازون Fluticasone (Cutivate)®
- بريدنى كاربيت prednicarbate (Dermatop)®
- تراى امسيلون Triamcinelone (Kenacort)®

4. Superpotent (> 1500)

- كلوبيتازول بروبيونات Ⓒ Clobetasol propionate 0.05% (Dermovate)®
- داى فلوكوترولون فاليرات Ⓓ Diflucortrolone Valerate (Nerisone fatty)®

Sideeffects of Topical Cs

(20) تذكر دا الكرس

. جدول مهم

- { Epidermal Atrophy
- Dermal Atrophy }
- steroid addiction synd
- Skin irritability & Fragility
- Striae
- purpura
- Telangiectasia (rebound VD)
- Hypo-pigmentat^.

- Hypertrichosis
- { perioral dermatitis
- periorbital → Cataract, Glucoma }
- { Acne Vulgaris
- Acne Rosacea } In Cognito
- ↑↑ { Exacerbat^ of Skin inf. ; " " Psoriasis }
- ↓ Delayed Wound healing.

- Systemic absorpt^ → ↑incid. ē:
  1. superpotent Cs
  2. children & Infant ??
  3. occlusion
  4. Wide spread use >50gm/W sup. or >100gm/W pot.
  5. Region eg delicate skin & Flexures
  → Commonest: HPA supp. [ليس عاماً] مع استخدام superpotent ((7.5gm/d))
- Tachyphylaxis
  - def. ↓ Cs effect ē prolonged use
  - May occur ēin 1W of ℞
  - To avoid: (shift to low potent) (use on holidays) (alternative ℞ eg Dovonex, TCI (Topical CIs))
- occlusion Complicat^
- Contact Dermatitis

- Discussion of Complicat^

استخدام الكريم " امن "

Cs induced Atrophy & effect on skin Layers

effect on epid.

- epid. thining occurs after: 1W of superpotent / 3Ws of potent
- ↓ thining; sp. St. Corneum
- ↓
  1. impair barrier funct^
  2. ↑ TEWL → Trans epid water loss
  3. ↑ irritability & Fragility.

effect on dermis

- ↓ Dermal vol. after 1-3 Ws of superpotent
- d.t
  1. ↓ hyalornic acid synth. by Fibroblasts
  2. ↑ Water loss
  3. ↓ Collagen synth. & ↓ elastin, ↓ fibroblast
- ↓
  1. dermal Atrophy
  2. striae
  3. Telangiectasia
  4. Fragility
  5. Purpura (d.t Poor vascular support)

Types (of Contact Dermatitis):

ICD	ACD
1. Frequent	less frequent
2. ± d.t propylen glycol	± Caused by: Cs itself, Vehicle, preservative, Fragrances
3. More ē Cream base [اتجدا مقدم دراهم أومن]	How to suspect: 1. Lack of efficacy 2. Worsening of Lesions

- patch test help sort out this problem.
- ACD more ē Hydrocortisone, Tixocortol & Less ē { Clobetasol, Mometasone, Betamethasone }

NB → Skin atrophy may be Reversible after stop.

. Steroid Addiction Synd.:

Mid-high or even Low potent] Cs applied to < Face / Genitals For several Ws → When discontinuing it → Sensat^ of < Burning / Severe itching (Symptoms of dermatitis that was treated by it in profound manner)

AE: thining of < St. Corneum / Epid → make the patient more susceptable to irritants

H: → discontinue Cs or gradual withdrawal & use of emollients & instruct the pt that symptoms may remains for (Ws--Ms) till complete cure.

(Qs)
- Moisturizers
- Soaps
- Sun screen
- Make ups

وقفة تراكمي

. occlusion complications:-

1- ↑ incid of systemic Abs.
2- bad odour
3- Miliaria
4- Folliculitis & infect^
5- Reversible atrophy of adjacent skin.

. Indications of Topical Cs

1- dermatitis
2- pLE
3- DLE
4- AA
5- lichen striatus
6- localized pemphigoid
7: إكزيما → Eczema ال

Contraindications

1- skin manifs. d.t Vaccinat^
2- Cut. TB & ✗
3- skin infect^s
4- Perioral dermatitis
5- Hypersensitivity.
6- Ps

6. Cut. dis not Responsive or Worsened by Cs:-

. all C.Is + Pit. Rosea, PRP, EM, Urticaria
. Dry skin & Ichthyosis, Large Vs Vasculitis, parapsoriasis

. Guidlines for use of Topical Cs

1. Acc. to potency
2. Acc. to Applicat^
3. Acc. to the Vehicle.
4. " " Amount

1. Super potent: ← on small area < 10% BSA, not > 2 Ws, not > 50 gm/W, No Under occlusion.
± used on Trunk & extremities
2. Potent ← not > 20% BSA, Not > 3-4 Ws, Not > 100 gm/W
(NB) ± used on Face for period < 2 Ws; ± used in children if failed lower Concs.
3. Mod potent → Tried on hand ecz & Atopy
4. Mild → used for chr. use in ← Face, Flexures, infants & children < 1Y.

---

2 Acc. to applicat

. Method → ↑ percut. Abs. by occlusion.
. Frequency → used in alternate day therapy
. Type of Cs (Tachyphylaxis): When using superpotent: use it 2/day for 2 Ws then Rest for 1 W & Repeat for 2 cycles (2 cycles) then → either
  1. Shift to lower potency
  2. use on holidays
  3. alternate therapy eg TCI (Tarolimus)

- يوصى في الاسبوع لمدة اسبوعين وارح اسبوع

3. Vehicle:

1. Oint → chr. dry lichenified lesion
2. Cream → Acute weeping dermatitis
3. Cream, gel, Alcohol & lot → hairy areas.

ترتيب سرعة الامتصاص:

- Oint
- Emollients
- Gels
- Cream
- Lot
- Sol.

4. Amount of Cs used:

1. determined by Fingertip Unit (FTU) ☜ is the amount of Cream expressed from a tube of 5mm diameter from the tip of index to the 1st distal joint. on Palmer aspect

2. 1 FTU = (0.5 gm) of medicat = will sufficient To treat 2 palm sizes in the average adult.

Site	FTUs
- Groin (or) hand	1
- Face or Foot	2
- one arm	3
- one leg	6
- Trunk (Front & back)	14

Neutrophilic Dermatoses (ND) (47)

(Neutrophilic Vascular Reactions)

def. inflammatory dermatoses ch. histopathologically by predominantly Neutrophilic infiltrates (Epid. or Dermal) in absence of infection or vasculitis & show prompt response to Cs

دہ تعریف: (. Sweet RD, Br. J Dermatol 64) (. Von den Driesch JAAD 94)

دہ تعریف (. Callen, Dermatol Clin . Lever, pathology 2002)

باعتبار ان على الرغم من أن الـ Vasculitis تتميز بالباثولوجي بتاعها Neutrophilic inf. cells ← بعض المؤلفين بيستبعدون Vasculitis من ND والآخرين بيعتبرونها نوع منه

Recent definition (Wallach & Vegnon-Penna 2006) (JAAD 2006)

(HL)

ND have 4 features:-

1. Non infectious cut. Neutrophilic infilt.
2. Potential Extra cut.
3. Frequent systemic associat.
4. possibility of an overlap bet. ND.

" والتعريف ده بيشمل الـ Vasculitis "

Classification of ND

1- Belognia classifi. (208) (السابق)
2- IJDVL classifi. (207) (HL)
3- Rook classifi. (راجع الإجماع للمذاكرة)

1- Bologna classif. for ND

(48)

Epid.

- pustular ps.
- AGEP
- SCPD
- IgA pemphigus < ؟؟
- Infantile Acropustulosis
- Transient Neonatal pustular Melanosis. (TNPM)
- keratoderma blenorrhagicum.
- Amicrobial pustulosis of folds.
  (♀ ē chr. pustulosis of : folds, EAC, scalp + CTDs.)

Dermal

With Vasculitis

- سمّيها براحتك Vasculitis
- Small V V.
- Med. V V
- Large V V

Without Vasculitis

- sweet synd.
- PG
- Behcet
- BADAS
- Neutrophilic
  - Eccrine Hidradenitis
  - Rheumatoid Neutrophilic dermatitis
  - SAPHO synd
  - Neutrophilic urticaria
  - Still's dis
  - periodic fever synds.
- Bullous dis:
  - DH
  - LAD
  - BSLE

"غير ND"

ALL HL

3 Neut: urtic, Eccrin, Rheum.

"Neutrophilic urticaria"

+/- Vasculitis

- Pustular Vasculitis of dorsal Hands.

سؤال أساسي

Acute febrile Neutrophilic dermatosis

(. Emed 2004 . Bologna . Andr. . Oamh . مذكرة) 4

(Sweet Syndrome)

(S.)

- Def.: Commonest ND (protype of all ND).
- Epidemiology: Age: . Typically → 30-50ys.
  - Some cases → Neonates ≃ 5 days.
- Sex . classical Type → M:F = 1:4
  - . Mg ass. & childhood → M = F.
- Race: → (No) predilect^n.
- Mortality / Morbidity ⇒ . depends on underlying cause
  - Most cases resolve spont. while others remains indefinitely
- ✓. Season: spring & Autumn
- pathogenesis: (1) Reactive process (to) Certain stimulia e.g < Mg / inf
  - (2) ± Ass. with:
    - Exogenous G-CSF
    - TNF
    - imbalance To Type I helper
    - HLA-B54
    - ✓ genetic predisposit^n
    - Ig & C → activat^n & Immobilizat^n of Neutrophils.

Revised Diagnostic Criteria (9)

(proposed by Su & Liu & revised by Von den Driesch) (1986)

(JAAD) (1994)

Major Criteria — clinical / HP

onset ① **Abrupt onset of:** Painful or Tender — Erythematous or Violaceous — Nodules or plaques — ± ē Vesicles, pustules or Bullae. Annular or arcuate.

Infilt. ② **predominantly dermal Neutrophilic infilt. without LCV.**

Minor Criteria

① ملحو of : تسبيقه < inf. vaccinat.
- Inf. — URTI, HCV, HIV, TB
  - URTI, ( )
  - GIT inf., or
  - Vaccinat. (BCG)
- Drug
- Mg ← Leuk. (AML)
- IBD
- AI CTD
- Pregnancy

② Fever > 38°C & Malaise

③ Lab findings: (≥ 3)
- ESR > 20.
- +ve CRP.
- Leukocytosis > 8000.
- > 70% Neutrophilia

?

④ Excellent response to CS or KI.

For Diagnosis:

Must → 2 Major + 2 Minor

بزاد oral ulceration → Mg + it's signification!

Syst Manifest → FAHM, CNS, CVS, Renal

← [Criteria of Mg sweet synd; Types + ass

CIP

(51)

Extracut.

① General:

- FAHM
- Arthralgia
- Myalgia

② Systemic organs affect:

- CNS → Headache, Consciousness (Transient (Not as Sheet)), Seizures, Meningitis, PN
- Pulm → dyspnea, Cough, Effusion, bronchiolitis
- Others: renal, GIT, bone

PuCo. Cut.:

Skin: → Nodules & plaques:

- Abrupt onset preceded by URTI
- Erythematous - Violaceous → Plum Colored
- asymmetrical on: Face, Trunk, arms (dorsal Hand)
- Painful or burning (then itchy) & Tender
- Sharply demarcated with an irregular (mamillated) Pseudovesicular or pustular surface & annular or Arcuate Config.

Variant: Vesicle, bullous

May show:
- pustules
- Bullae
- ulcers

Vesiculobullous

Targetoid +ve Pathergy Test.

- Fate: resolution either Spont. or with ↓↓ without scarring but re currence is common. 30-50% (classic) (Mg ass.)

MM:
- oral: → ulcers (Common in Mg ass.)
- Eye: → Conjuctivitis & Episcleritis, Uveitis, retinitis, ...

Clinical Varieties of Sweet

Idiopathic

1. Classical (Common) Type (70%)
2. Inflammatory dis. ass. (infarctos) (15%)
3. Neoplasm ass. (Mg) (10)
4. Preg. ass. (2%)
5. Localized (Face) [cellulitis] or Hands

Conditions may be ass. with Sweet synd:

- Inf. & Vaccinat.
- Mg.
- Drugs.
- IBD
- AI-CTD

A. Frequent:

1- Infection:
- URTI d.t Strept
- GIT Yersiniosis, HCV, HBV

2- Mg:
- Commonest → Hematological (10-20%) Specially AM Leukemia
- Less common → Solid Tms es Cancer:
  - Bladder
  - Breast
  - Colon
  - Genital

3- IBD

4- Drugs: G-CSF, (Doxy, Retinoids)
Frusemide, Azithro.

B. less frequent:

- Inf.: TB, HCV, HIV, CMV
- Vaccinat → BCG
- Autoimmune → RA, SLE, DM, SS.
- Drugs:
  - Frusemide
  - Hydralazine
  - Sepetrin
  - Retinoids
  - Doxy
  - Azath.
  - OCPs.

Investigations:
1. Lab: Non Specific
   - as ESR & CRP
   - Leukocytosis > 8000
   - Neutrophilia > 70%
2. Rad: عشان نستبعد الأسباب الداخلية
3. Histopathology: (Tri d)

A. Neutrophilic infilt: dense, diffuse (in) reticular dermis.

Also Massive upper papillary derma Edema.

B. Lymphocytic debris

C. Vascular damage → No Vasculitis (Ng LCV)

Treatment

8

34

1) العلاج الاساسي ← (Cs)

(0.5-1 mg/kg/d for 4-6 Ws)

2) البدائل:

- KI (900 mg/d)
- Dapsone (100-200 mg/d)
- Colchicine (1.5 mg/d)
- NSAIDs; Indomethacin.

ويمكن تذكر أن هذا المرض:

1) Bg condition; if untreated it well remains Ws - ms.
   ↓ برلينيا (5-12 Ws)
2) Cut lesions → involute Ē out scarring
3) Recurrence: (نأتي الربيع الحزين ?)
   - Ē classical cases → 30% (Even ē ttt)
   - Mg ass. → 50%
4) Treat URTI

NB:

Characteristic features of malignancy-associated Sweet's syndrome

1- (No) < sex predilection (M = F)
   URTI
2- Blood – Anemia
   – Thrombocytopenia
   (–Ve) Neutrophilia in ≥ 50%
3- Lesion: appears → Before Mg (60%)
   - Severe wide spread.
   - Bullous or ulcerative & oral mm. affect
   - Highly recurrent (≈ 50%) & often herald Tm relapse.

Acute febrile neutrophilic dermatosis is a misnomer?

- Chronic recurrent forms exist.
- Fever and neutrophilia are variable features.
- Extracutaneous manifestations are common.

DD
برلينيا
383

Pyoderma Gangrenosum (PG)

(56)

Def.: uncommon, recurrent, chr. cut. ulcerative dis with distinctive Morphologic presentation.

Pathophysiology: unknown but may be dysregulation of immune system specially: altered Neutrophil chemotaxis is believed to be involved.

Epidemiology: . Age: . Commonest: 20-50 ys;

. 4% of cases: Infants & children.

. Sex: } No predilection to specific sex or race.
. Race: }

CIP

A- Typical Presentation → ulcerative P.G.

B- Atypical presentation:

- Bullous (atypical or vesiculobullous)
- pustular
- Vegetative (superficial granulomatous).
- Mg

white:
- oral (Pyostomatitis Vegetans)
- Genital
- peristomal
- childhood

- Extracut. (systemic)

Rook (Ch 49.38) → • PG ass. e Novel ANCA To azurocidin. ✓

Pyoderma Gangrenosum

For diagnosis: 2 Major + 2 Minor

pain, size, course

Major criteria (both required)

1- Rapid (usually > 1 cm/day) progression of painful necrolytic ulceration with an irregular, undermined, violaceous border, usually with a preceding papule, pustule or bulla, and pain out of proportion to the size of the ulcerated area.

2- Exclusion of other causes of ulceration.

Minor criteria (at least 2 required)

1. (a) history of pathergy, or (b) presence of cribriform scarring.
2. Presence of a disease known to be associated with PG (IBD, polyarthritis, myelodysplasia, leukaemia, monoclonal gammopathy).
3. Appropriate histopathological findings. (H/p)
4. Rapid response to oral corticosteroid therapy (usually interpreted as at least 50% reduction in size using 1-2 mg/kg/day). within (1 m)

Classification of PG

Morphologically

① Ulcerative = (Typical)	② Bullous	③ Pustular	④ Vegetative
Frequent	Frequent	Frequent	Uncommon
Arthritis, IBD, monoclonal gammopathy	Hematologic dyscrasias/ Malignancy	IBD	No systemic associations/ Chronic renal impairment
Lower limbs	Upper limbs	Face and trunk	Trunk

ass → (IAG) · IgA Benign →

?? WG or PG

⑤ Mg : Head Neck

⑥ genital

⑦ oral

⑧ peristomal

⑨ Extracut = systemic

- IBD : 20-30
- Arthritis : RA - or Sero-Ve (20%)
- IgA : 15% (Plasma Cell dyscrasia)

Clinical types	Histopathology
Ulcerative [Figure 5] →	Edema, neutrophilia Secondary lymphocytic vasculitis
Bullous →	Epidermal necrosis with neutrophils. subepidermal bulla
Pustular →	Epidermal and dermal neutrophilia
Vegetative →	Neutrophilic and eosinophilic and histiocytic mixed infiltrate. Intra- and subepidermal granuloma formation

N + E + H

Syndē PG:

- PAPA
- PASH : PG, Acne, S-Hidradenitis.
- PAPASH : PAPA + Supp. Hidradenitis.

Typical (Ulcerative) PG (57)

- Site: Legs (pretibial) (but ± any site).
- Ass: (التركيب)
  - IBD
  - Arthritis
  - Mg (Lymphoproliferative)
- Ch: start as painful papulopustule / Nodule or Bulla on Erythematous violaceous induration.

Necrosis → Ulcer (ulcer أي)

1- عددها: Single or multiple
2- depth: shallow or deep (Tendon or ms. يعني مش جلد)
3- Border: Border (rim): Gun metal = Cyanotic or livid (مزرق أو مائل للأزرق)
4- edge: Edge: undermined
   - Extends Centrifugally.
- Floor: Floor: Purulent, GT or Necrosis. Atrophic
- Healing: Healing: Cribriform, ± pigmented scar

Diagnostic Criteria (IJDermatol, 2004)

- *Major criteria (both required)* → or 50% in size in 1 month
  1- Rapid (usually > 1 cm/day) progression of painful necrolytic ulceration with an irregular, undermined, violaceous border, usually with a preceding papule, pustule or bulla (pain out of proportion to the size of the ulcerated area.)
  2- Exclusion of other causes of ulceration.
- *Minor criteria (at least 2 required)*
  1- (a) history of pathergy, or (b) presence of cribriform scarring.
  2- Presence of a disease known to be associated with PG (IBD, polyarthritis, myelodysplasia, leukaemia, monoclonal gammopathy).
  3- (HP) (##) Appropriate histopathological findings. (sterile dermal Neut. (±) mixed inflamm / lymphocytic vasculitis)
  4- Rapid response to oral corticosteroid therapy (usually interpreted as at least 50% reduction in size using 1-2 mg/kg/day in 1 month)

(58) **ATypical Variants of PG**
[• Site • Ass • Ch]

1- Vesiculobullous (Bullous or ATypical PG):

- Site: Face & UL (Extensors & dorsal Hands) → DD from Sweet's.
- Ass.: Lympho proliferative disorders.
- Ch: Hgic bullae.

(HL) NB → Vesiculopustular (Juicy) Component may be at the border.

2. Pustular:

- Site: Extensors of limbs & Trunk
- Ass: IBD
- Ch: usually regress (without) scarring but may Evolve into (Classical PG) (Seen during exacerb. of Classical Type)

رجلة وتتحول لـ classical
تحت لعلاج IBD ← (IH)

3- Vegetative (Superficial granulomatous): ← أخطر

- Site: Trunk
- Ass.: → (No) Ass.
- Ch: By: ① Solitary ② Slowly progressing then resolve c̄ less aggressive Rx. (Topical Rx)

4- Malignant:

- Site: Head, Neck & upper Trunk.
- Ch: Not known whether it is Variant of Typical PG (Head & Neck Variant) or it's cut. presentat. of WG to diff.?? (CANCA) -ve it's ch For WG but -ve cases of WG are present so follow up For RT or Renal affect. — تشخيص مهم

5. Oral PG (Pyostomatitis Vegetans):

- Site: labial & buccal Mucosa.
- Ass: IBD
- Ch: . Chr. sterile (Vegetative) Pyoderma
  . ± ass. with Ulcerative (or) Vegetative PG.

6. Genital PG: at Vulva, penis & scrotum.

7. Peristemal: . PG around (stoma) sites of resected IBD or GIT or UB Cancer
   . DD: around irritat° or inf.

8. Childhood PG: as in adult but tend to affect: . Head
   . Genitalia
   . Perianal.

Sweet. is → 9. Extracut PG: Extra cut. Neutrophilic infilt. reported in:
- Eye
- Lung
- GIT
- Bone

Associated Conditions

- 50-70% of PG Cases Have antecedent (or) Coincident ass. diseases or Conditions as:

1. IBD 20-30% (Chron's & U. Colitis)
2. Arthritis 20%
   - RA sero-ve → ndylitis of IBD
3. Hematological Mg: (15-25%)
   - Leukemia:
     - AM
     - CM
     - Hairy cell
   - Gammopathy (15% sp IgA) usually Bg.
4. PAPA Synd:
   - Pyogenic sterile arthritis
   - PG
   - Acne.

   → d.t Mutat° in (CD2) binding protein → abNL inflamm response
5. other ass. Neut. dermatoses e.g BD, SCpD.

Histopathology :-

(6)

لو شكيت فيها اكلينيكيا
أعمل
- pathergy

- usually non specific (specially) if PG is mild or Treated & Biopsy indicated to Exclude other Conditions. « Diagnosis of PG of D of Exclusion »

- ✓ Epid. & Dermal Necrosis & ulceration sur. by — 2 Types of infilt. — Acute: intense Cell infilt. / Chr. peripheral Cell Infilt.
- Classical Type: massive Epid. & Dermal Neut. Infilt. ē Abscess format.
- Bullous: Intraepid. Vesicles ē Neut. Infilt.
- pustular: Perifollicular & Subcorneal Neut. Infilt.
- Vegetative: Granulomatous react. ē palisading

أهم ٣ — Cs / Ciclosporin / Thallidomide

Treatment of PG:

قاعدة « There is Neither specific Nor uniformly Effective Tt ».

Best is Cs (Topical & systemic)

Best lines (Evedince based)	Book author's openion
Topical (2): - IL Cs & Topical; - Tacrolimus; - IL Cyclosporine	Best Tt For PG ass. ē IBD or arthritis
Systemic (2) ✓: • Antibiotics; • Dapsone; • Sulfasalazin; • Lamperen; • Cs — oral / pulse; • Cyclosporin (مهم); • MTX; • Azathioprin	MTX + Cs or Anti TNF.

DD
1. Inf.
   - Ecthyma
   - TB ulcer
   - Deep ...
2. Vascular
   - Venous & arterial ulcers.
3. Mg: leuk. & lymph.
4. Tissue injury: Artefact

Behcet disease (BD)

(61)

(Oculo-oral-Genital Syndrome)

def. Multisystem dis. ch by:

- skin
  - oral ulcers
  - Genital ~
  - pustular vasculitis
- Eye → ⊙ Uveitis.
- joint → ⊙ Arthritis.
- CNS. → ⊙ Meningoencephalitis.

Etiology: unknown but may be d.t:

1- **Genetic** → Significant ass with HLA B $\begin{matrix}5\\51\end{matrix}$ or
- Little ass. of HLA B27

+ve FH (10-15%)

2- **Immunological** (Type III React.): supported by Evidence of Immune complex deposit & Vasculitis.

3- **Infection:** → HSV, HCV & Strept.

4- **Allergy** → food allergy is suggested e.g Wal(nuts)

Epidemiology: Age: any, including Neonates but peak is at 20-35 yrs

Sex: M > F.

BD may be Classified as

- **ND or Neutrophilic Vascular reaction** → become its early lesions show Neutrophilic infilt. (cut) Vasculitis
- **pustular Vasculitis:** Fully developed lesions show Vasculitis (Fibrinoid deg. & Necrosis) & if it occurs acc. by severe Neutrophilic infilt so called (Pustular)

Behcet Disease

1-Diagnostic criteria according to ISG (International study group for Behçet's Disease .1990)

Criterion	Required features
Recurrent oral ulceration	Minor aphthous, major aphthous, or herpetiform ulceration observed by physician or patient, which recurred at least 3 times in one 12-month period
Plus any two of the following:	
Recurrent genital ulceration	Aphthous ulceration or scarring, observed by physician or patient
Eye lesions	Anterior uveitis, posterior uveitis, or cells in vitreous on slit lamp examination; or Retinal vasculitis observed by ophthalmologist
Skin lesions	Erythema nodosum observed by physician or patient, pseudofolliculitis, or papulopustular lesions; or Acneiform nodules observed by physician in postadolescent patients not on corticosteroid treatment
Positive pathergy test	Read by physician at 24-48 h.

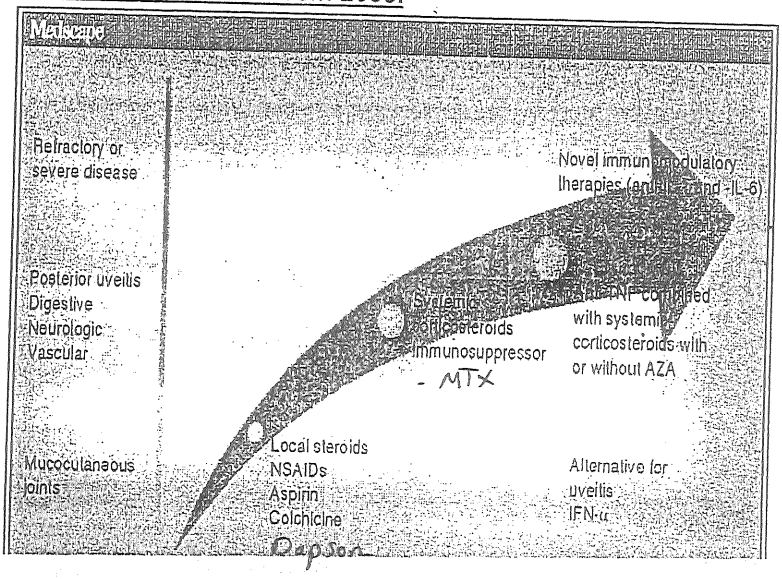
2-

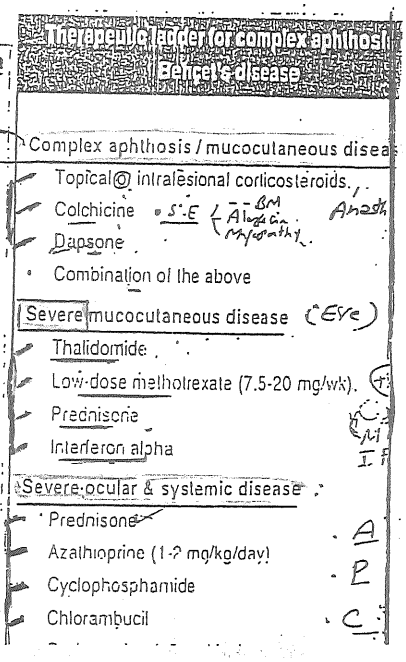
International criteria for the diagnosis of Adamantiades-Behçet disease (2014) (9)

Recurrent oral aphthous ulcers	2
Skin lesions (papulopustules, erythema nodosum, thrombophlebitis)	1
Vascular involvement (arterial or venous thromboses, aneurysms)	1
Recurrent genital aphthous ulcers	2
Ocular involvement (hypopyon-iritis, uveitis)	2
CNS involvement (meningo encephalitis)	1
Positive pathergy test	1

Adamantiades-Behçet disease 4 or more points

- Lines of TTT : According toThe European League Against Rheuma recommendations from 2008.





C/P of BD

1- Recurrent oral ulcers:

كام مرة؟ — سؤال الرئيسية !! Recurrent يعني → recur ≥ 3 times / y (Either reported by patient or reliably physcian).

- usually: painful.
- Types.

قرح فم متكررة مماثلة تماماً لقرح الفم العادية

Minor →	1-5, small (≤10 mm); moderately painful; resolve ē in "4-14 d's" without scar (scarring only in 10%)
Major →	1-10 large (10-30 mm); very painful; persist upto 6 ws → scar (60%); High incid of Antimucosal Abs
Herpetiform →	Recurrent crops of as many as 10-100 small (1-3 mm) painful ulcers. Heal: within 4 ws ē scarring. Low incid. of Anti mucosal Abs in 30%

2- Recurrent Genital ulcers:

✓ similar to oral ulcers but differs in:
- More larger & painful.
- More deeper ē irregular border.
- Heal ē scarring.

- reported either by physcian (or) reliably by the patient

- Site:

♂	♀
Commonest: Scrotum	- Vulva
other: penis.	- Vagina
	- CX

بالترتيب

مميزة لقلة الإمراض اللي بـ (Scrotal ulcers) ← Commonest Scrotum

NB: ± epididymorchitis.

5. Eye manifs: (9%)

- Most common: post Uveitis & Retinal Vasculitis.
- others: ant. Uveitis
  - Hypopyon
  - Glaucoma
- Eye affect is the leading cause of Morbidity as it may → blindness.

6. Other Systemic manifs:

A. Arthritis: (80%)
- Mono or poly.
- Non Erosive
- site: Knee, wrist & ankle.

B. GIT: (5%) Br
- Pain, vomiting, dist., etc...
- ulcers!

C. CNS:
- occurs during evolution of dis.
- of poor prognosis
- includes: · meningoencephalitis
  · Cranial N. palsies.

D. Vascular: BD may affect:
- occlusion
- aneurysm

Larger:
- Arterial occlusion → pulm. & subclavian
- Venous → SVC, IVC & Femoral

Smaller:
- Meningo-encephalitis & GIT ulcers.

- Varices
- Aneurysm

Pulm. aneurysm & Embolism → Hemoptysis

Vascular complications don't respond to medical Rx.

Behcet EN like lesion!! DD
. EN
Thrombo-phlebitis.

3. Skin lesions:

. Dust ⟶ Pustular vasculitis (papulopust. or vesicu. pustula)
⟶ EN like lesions (more in ♀).

. Others:
. Sweet like
. PG like
. Pseudofolliculitis
. Acneform nodules (ē no Hx of Cs).

Pathergy Phenomena??
occurance of ND lesion at site of Trauma

4. Pathergy test:

. Def. Hypersensitivity test ō demonstrate ↑ neutrophil chemotaxis at site of Trauma. (..... Koebner phenomena of LP)

. Method:

. Needle prick of ID injection of 0.1 ml saline or histamine ⟶(1-2 ds) Erythematous papule or sterile pustule (> 2mm)

lep ☒
تفاصيل الإبرة:
20-22 gauge
تغرس الإبرة بشكل
ليس عمودي
نحو 5mm
Flexor forearm

. Results: . may be +ve ↗
or
−ve ⟶ repeat at 2-5 points before results are accepted

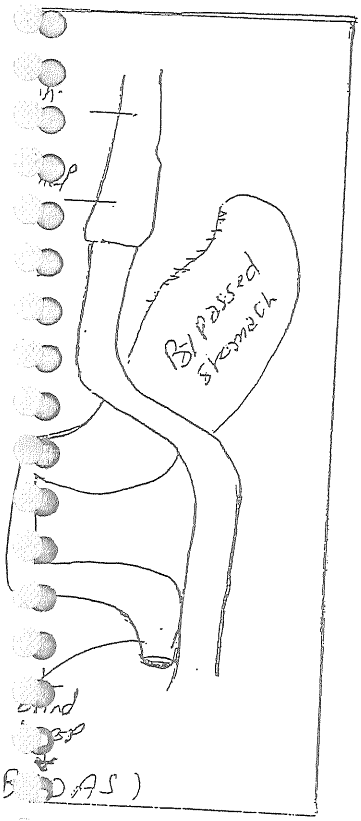
. Test ch by:
. High +ve (≃ 90%) → Middle east
. weak +ve (≃ 50%) → Far east
. Much " " → Western.

. This test is +ve in ND:
. Sweet
. PG
. BD

Bowel associated Dermatosis Arthritis Syndrome (BADAS). (66)

(Bowel by pass Synd)

ممكن تحدث في ٤ حالات



1. **By-pass operation to Create blind loop as:**
   - Jejunoileal by-pass Surgery
   - Gastric by pass "

   ع عملية السمنة المفرطة "PU"

2. Bilio pancreatic diversion
3. IBD
4. Diverticulitis

↓

Bacterial over growth in the blind loop → release of Bacteria Ags (as peptidoglycans) → Immune complex Formation → deposition in Skin & Joint.

↓ (1-6 yrs) بعد العملية

Manifs of BADAS: مهم

A. Cut. manifs. (Dermatosis = ND):

1. **Usually:** Erythematous macules → papules → purpuric vesiculopustules (within 48 hrs)

   تظهر ع سنين وتختفي وترجع بعد شهر وهكذا

   Commonest sites: Extremities & trunk.

2. **Other lesions:** Erythematous S.C Nodules as ±:
   - EN or Nodular non-Suppurative Panniculitis

   DD →

Nodular non Supp. Panniculitis
- Scarring (depressed)
- lobular
- at legs, buttocks & abd.

B. Arthritis

(67)

- Arthralgia
- Non Erosive Polyarthritis
- Tenosynovitis

C. others

- General Manif → Serum sickness like (FAHM), Myalgia.
  - diarrhea
    - Zinc, vit A, deficiency
  - Hepatic dys f.
  - renal Calculi.
- Histopathology → Very similar to < Sweet / PG (Early) / Behcet.
- Treatment: → Bologna table 27.12 (p. 391)

Antineutrophil drugs

- Antibiotics
- Colchicin
- Dapsone
- thalidomide
- CS
- other Immunosuppressives

Neutrophilic Dermatosis (Pustular Vasculitis) of dorsal Hand

(68)

- Some Consider it as a localized variant of Sweet Syndrome.
- Clp Edematous ulcerative or pustular Nodules & plaque at dorsal Hands.
- Path. : as Sweet but there may be Lcv.
- Ht : as Sweet.

Neutrophilic Eccrine Hidradenitis

def. ND ch. by inflamm. of Eccrine sweat gland.

Clp :

غالباً تحصل بعد جلسة كيماوي
وخصوصاً (Cytarabin) لمرضى الـ AML
Leukemia & Lymphoma علاج حالات الـ
وغالباً تبدأ في المرض عند Neutropenia.

- lesion Acral : Erythematous, Edematous, papules, plaques, Purpura & pustules located at
  - Face → (Periorbital) عند
  - Palms
  - Extremities.
- There may be fever.

Ht →
- NSAIDs
- Dapsone
- Cs.

Extracut ND (MedsCape.com → xCeltat).

- Commonest ulcerative dis. of the oral cavity. affecting at least 20% of the population.
- Ch-BY: → Recurrent episodes of small, round or ovoid ulcers ē circumscribed margins, erythematous halo & yellow or grey floor.
  ↓
  Healing occur ēin (1-2) ws

(margin: pharyngitis, adenitis, aphthous)

- AET → Many predisposing factors
  1. Behcet's dis.
  2. Hematological deficiencies ← Iron, Folic acid, Vit-B12
  3. Malabsorpt° e.g Coeliac & Crohns.
  4. Trauma, Certain food, Stress & Cessation of smoking. ← "Nicotine-replacement Rx"
     ↓
     CMI Role postulated but it is controversy.
  5. Idiopathic
  6. Inf. ← Strept, H. pylori

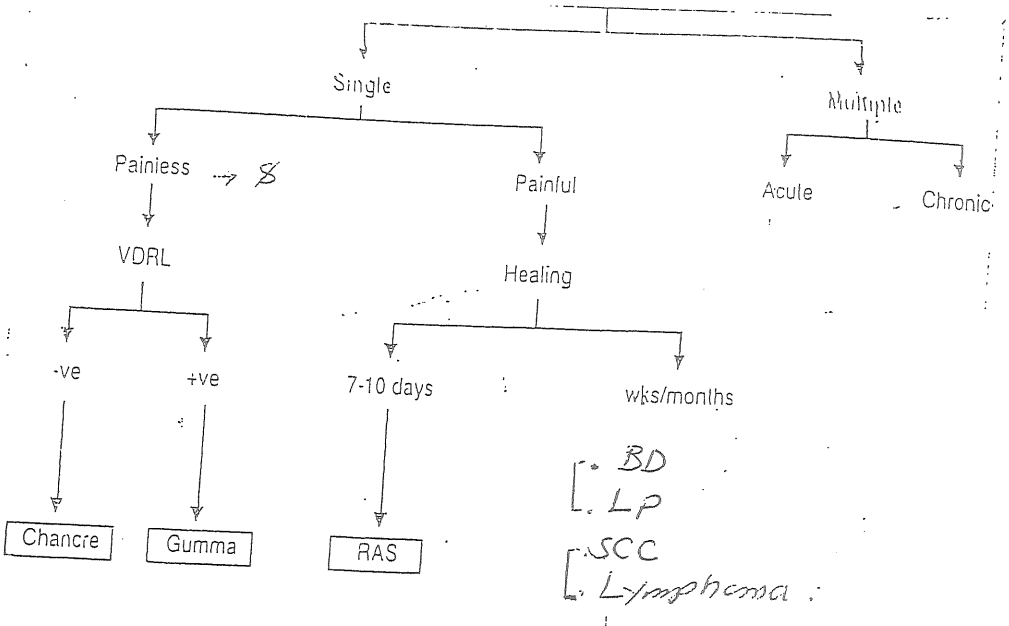
(margin: Stress, Smoking, Trauma, Food)

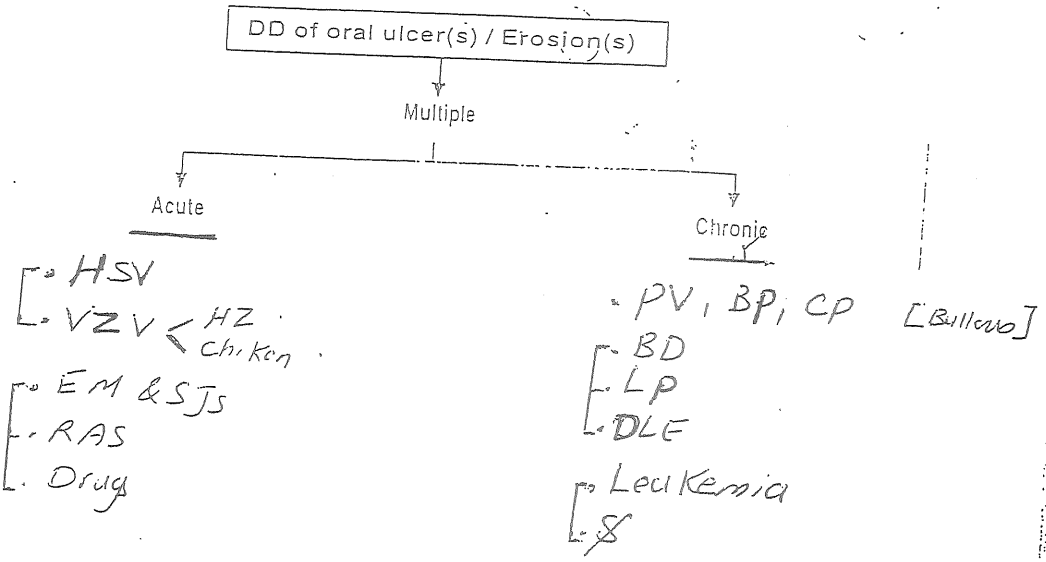
Characteristics of the three variants of recurrent aphthous stomatitis

Characteristic	Ulcer type: Minor aphthous	Major aphthous	Herpetiform
Incid → ~~Female:Male~~ ratio	1.3:1 (F>M)	0.8:1 (M>F)	2.6:1 (F>M)
Age of onset	Childhood or adolescence	Childhood or adolescence	Young adult
No. Lesions:			
Size	<10 mm	>10mm	1-2 mm
Site (location)	Lips, cheeks, tongue	Lips, cheeks, tongue, palate, pharynx	Entire oral mucosa
Number	1-5	1-3	10-100
Duration of each ulcer	Up to 10 days	Up to 1 month	Up to 1 month
Healing with scarring	10%	50%	30%
Prevalence	80% "most common"	10%	10%

(TH)
1. Exclude systemic dis.
2. Rx of predisposing factors
3. Topical Tetracycline mouth wash., Anaesthetic, Co... Topical ← Dermovate, Amlexanox, Sucralfate
4. Thalidomide, Dapsone & Colchicine., Montelukast, Azathioprine

FDA in Major type of HIV — 50 mg/d





Complex Aphthosis: ≥ 3 oral ulcers + Genital ulcers but No systemic Manifs. of BD

oculomucocut Synds (DD of BD)

- BD (Behcet)
- EM
- Sweet
- Reiters
- PV
- CP
- ✗
- HSV
- LE
- MCTD

Eosinophilic dermatoses (75)

(disorders ch. by Predominant Eosinophilic infilt.) ± peripheral Blood Eosinophilia)

1. Well's synd
2. Granuloma Faciale
3. Hypereosinophilic synd.

• Well's Syd (Eosinophilic cellulitis)

- Chr. recurrent Cut. disorder ch <
  - Clinically by: Cellulitis like rash
  - pathologically by: Flame figures.

- Etiopath.:
  - Arthropod bites
  - Infect / Infest. → Viruses, Tinea, Toxocara canis.
  - Myeloprolif.

- Epidemiology: Adults, without predilect.

- C/P: itchy or burning, indurated Erythematous Nodules & plaques (cellulitis like) —4-8 w→ Faint-pink, brown or slate gray pigm. on limbs → recurrence.

- There may be <
  - FAHM, Eosinophilia.
  - Clinically Varieties: Papules, Vesiculobullous & Annular.

(Path) Deep dermal (± SC or fascia) Eosinophilic infilt. + Flame figures [Collagen coated by Eosinophilic granular proteins].

(Lab) • Blood <
- ↑Eos.
- ↑Eos. cationic ptn.
- ↑IL5

• Toxocara canis (∅): < Stool, IgE, antibodies.

DD <
- (Clinically) → See pseudocellulitis & cellulitis.
- (Path) → Causes of Flame figure: Arthropod bite, scabies, Eczema, Drug Erupt. & Mastocytomas, Sweet.

Tt:
- Cs: 10-80 mg/d tapered over 1m. → dramatic Response
- Others: Topical Cs, Dapsone, Minocycline, Griseofulvin & Antihistamines.

Granuloma Faciale (GF) (76)

(Def) Chr., Bg (± self limiting), Idiopathic skin disorder CL by single or Multiple red-brown Cut. Nodules on face.

(Etiopathog.) ??

(Epidemiology) Middle age ♂ > ♀

. C/P : . Single, Asymmt., Smooth red-brown or Violaceous Plaque on (Face) c̄ (prominent follicular opening). (مهم)

. Varieties:
- Multiple lesions.
- papular lesions.
- Extrafacial GF.
- Nasal involvement (Eosinophilic angiocentric Fibrosis)

(Course)
- (No) Associated systemic Manifs.
- (±) resolve spont.

. (Path.) (٣ حاجات)

. diffuse Mixed dermal Infilt. ← E., N., L.

. LCV (±)

. GrenZ Zone.

. (DIF) +ve deposition at Vs. wall ← IgG, IgA, IgM & C3.

(DD) ① SL. ② Sarcoidosis. ③ Granulomatous rosacea

④ EED. (difficult to Diff. from Extrafacial GF; by:
- over Joints
- Neut > Eo.
- LCV)
- No Grenz
- Epid chang

(Rx) (often resistant)

. 1st line: IL Cs.

. 2nd line:
- . Dapsone
- . Clofazimine
- . Tacrolimus
- . PUVA
- . ... laser.

Hypereosinophilic Synd (HES)

(77)

Diagnostic Criteria:

1. peripheral Blood Eosinophilia > 1500 /ul for > 6 ms (or < 6 ms but ± evidence of organ involvement).

2. Absence of other cause of Eosinophilia e.g. (Hyper)

3. Evidence of organ involvement (Thus excluding By Eosinophilia)

Types 1. Myeloproliferative.

2. Lymphoproliferative..

Mucocutaneous lesions (30% of cases)

- pruritic Erythematous papules or Nodules.
- Urticaria & Angioedema
- Mucosal Failure

Cause of death CHF.

Rx: - Cs
- Imatinib